Please amend the above-identified application as follows:

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1. (original) A composition for inhibiting the function of a target polynucleotide sequence in a mammalian cell, wherein said composition comprises an agent that provides to a mammalian cell an at least partially double-stranded RNA molecule that does not produce a functional protein, and that comprises a polynucleotide sequence of at least about 200 nucleotides in length, said polynucleotide sequence being substantially homologous to said target polynucleotide sequence, and substantially non-homologous to a selected naturally-occurring, essential mammalian polynucleotide sequence.

2. (original) The composition according to claim 1 wherein at least 11 contiguous nucleotides of said polynucleotide sequence of said RNA molecule are present in a double-stranded sequence, depending upon the composition of said polynucleotide sequence and a ΔG of about -9.2 kcal/mol.

3. (original) The composition according to claim 2 wherein substantially the entire polynucleotide sequence of said RNA molecule is double stranded.

4. (original) The composition according to claim 1 wherein said RNA molecule polynucleotide sequence has a sequence of between at least about 12 to about 16 contiguous nucleotides in exact homology to said target polynucleotide sequence, and wherein said overall homology of said RNA molecule polynucleotide sequence to said target sequence is greater than about 10%.

5. (original) The composition according to claim 4, wherein said homology is greater than about 50%.

6. (original) The composition according to claim 1 wherein said agent is an RNA molecule made by enzymatic synthetic methods or chemical synthetic methods *in vitro*.

7. (original) The composition according to claim 1 wherein said agent is an RNA molecule made *in vitro* by isolation from a recombinant microorganism or the culture media in which said microorganism is grown.

8. (original) The composition according to claim 1 wherein said agent generates said RNA molecule *in vivo* after delivery to said mammalian cell.

9. (original) The composition according to claim 1 wherein said agent is a double stranded RNA.

10. (original) The composition according to claim 1 wherein said agent is a single stranded RNA sense strand.

11. (original) The composition according to claim 10 wherein said single stranded RNA sense strand forms a hairpin at one or both termini or intermediate between said termini.

12. (original) The composition according to claim 10 wherein said single stranded RNA sense strand folds back upon itself to become partially double stranded.

13. (original) The composition according to claim 1 wherein said agent is a single stranded RNA anti-sense strand.

14. (original) The composition according to claim 13 wherein said single stranded RNA anti-sense strand forms a hairpin at one or both termini or intermediate between said termini.

15. (original) The composition according to claim 13 wherein said single stranded RNA anti-sense strand folds back upon itself to become partially double stranded.

16. (original) The composition according to claim 1, wherein said agent is a single stranded RNA sequence comprising both a sense polynucleotide sequence and an anti-sense polynucleotide sequence, optionally separated by a non-base paired polynucleotide sequence, said single stranded RNA sequence having the ability to become double-stranded.

17. (original) The composition according to claim 1 wherein said agent is a circular RNA molecule that forms a rod structure.

18. (original) The composition according to claim 8 wherein said agent is a double stranded DNA molecule encoding said RNA molecule.

19. (original) The composition according to claim 18 wherein said DNA encodes a double stranded RNA.

20. (original) The composition according to claim 18 wherein said DNA encodes a single stranded RNA sense strand.

21. (original) The composition according to claim 20 wherein said DNA encodes a single stranded RNA sense strand that forms a hairpin at one or both termini or intermediate therebetween.

22. (original) The composition according to claim 20 wherein said DNA encodes a single stranded RNA sense strand that folds back upon itself to become partially double stranded.

23. (original) The composition according to claim 18 wherein said DNA encodes a single stranded RNA anti-sense strand.

24. (original) The composition according to claim 23 wherein said DNA encodes a single stranded RNA anti-sense strand that forms a hairpin at one or both termini or intermediate therebetween.

25. (original) The composition according to claim 23 wherein said DNA encodes a single stranded RNA anti-sense strand that folds back upon itself to become partially double stranded.

26. (original) The composition according to claim 18 wherein said DNA encodes a single stranded RNA sequence comprising both a sense polynucleotide sequence and an anti-sense polynucleotide sequence, optionally separated by a non-base paired polynucleotide sequence, said single stranded RNA sequence having the ability to become double-stranded.

27. (original) The composition according to claim 18 wherein said DNA encodes a circular RNA molecule that forms a rod structure.

28. (original) The composition according to claim 1, wherein said agent is a plasmid.

29. (original) The composition according to claim 1, wherein said agent comprises a first DNA plasmid encoding a single stranded RNA sense polynucleotide sequence and a second DNA plasmid encoding a single stranded RNA anti-sense polynucleotide sequence, wherein said sense and anti-sense RNA sequences have the ability to base-pair and become double-stranded.

30. (original) The composition according to claim 28, wherein said plasmid comprises bacterial sequences.

31. (original) The composition according to claim 1, wherein said agent is a recombinant bacterium.

32. (original) The composition according to claim 1, wherein said agent is a recombinant virus.

33. (original) The composition according to claim 1, wherein said agent is a donor cell transfected in vitro with the molecule described in any of claims 2 through 32.

34. (original) The composition according to any of claims 30-32, wherein said agent is selected from the group consisting of a living recombinant virus or bacteria or cell, a dead virus or bacteria or cell, or an inactivated virus or bacteria or cell.

35. (original) The composition according to claim 1, wherein said agent lacks a poly-adenylation sequence.

36. (original) The composition according to claim 1, wherein said RNA molecule is not translated.

37. (original) The composition according to claim 1, wherein said agent lacks a Kozak region.

38. (original) The composition according to claim 1, wherein said agent lacks an initiating methionine codon.

39. (original) The composition according to claim 1 wherein said RNA molecule lacks a cap structure.

40. (original) The composition according to claim 1 wherein said agent lacks signals for protein synthesis.

41. (original) The composition according to claim 1, comprising a mixture of different said agents.

42. (original) The composition according to claim 1 wherein said target polynucleotide sequence is a virus polynucleotide sequence necessary for replication and/or pathogenesis of said virus in an infected mammalian cell.

43. (original) The composition according to claim 42, wherein said virus is selected from the group consisting of a DNA virus and a virus that has an intermediary DNA stage.

44. (original) The composition according to claim 43, wherein said virus is selected from the group consisting of Retrovirus, Herpesvirus, Hepadenovirus, Poxvirus, Parvovirus, Papillomavirus, and Papovavirus.

45. (original) The composition according to claim 44, wherein said virus is selected from the group consisting of HIV, HBV, HSV, CMV, BPV, HTLV and EBV.

46. (original) The composition according to claim 1, wherein said target polynucleotide sequence is a tumor antigen or functional fragment thereof or a regulatory sequence of a virus-induced cancer, which antigen or sequence is required for the maintenance of said tumor in said mammal.

47. (original) The composition according to claim 46, wherein said cancer is selected from the group consisting of HPV E6/E7 virus-induced cervical carcinoma, HTLV- induced cancer and EBV induced cancer.

48. (original) The composition according to claim 1, wherein said target polyrucleotide sequence is a polynucleotide sequence of an intracellular or extracellular pathogen necessary for replication and/or pathogenesis of said pathogen in an infected mammalian cell.

49. (original) The composition according to claim 1 wherein said target polynucleotide sequence is a polynucleotide sequence of an abnormal cancer-causing sequence in a mammal which also possesses a normal copy of said sequence, and wherein the differences between the abnormal and the normal sequences are differences in polynucleotides.

50. (original) The composition according to claim 49 wherein said abnormal sequence is a fusion of two normal genes.

51. (original) The composition according to claim 50 wherein said target polynucleotide is the polynucleotide sequence spanning said fusion.

52. (original) A pharmaceutical composition comprising a composition of any of claims 1-51, and an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier.

53. (original) The composition according to claim 52, wherein said second agent is selected from the group consisting of a local anaesthetic, a peptide, a lipid including cationic lipids, a liposome or lipidic particle, a polycation, a branched, three-dimensional polycation, a carbohydrate, a cationic amphiphile, a detergent, a benzylammonium surfactant, or another compound that facilitates polynucleotide transfer to cells.

54. (original) The composition according to claim 53 wherein said second agent is bupivacaine.

55. (original) A method for treating a viral infection in a mammal, comprising: administering to said mammal a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a virus polynucleotide sequence necessary for replication and/or pathogenesis of said virus in an infected mammalian cell, in an amount effective to reduce or inhibit the function of said viral sequence in the cells of said mammal.

56. (original) A method for preventing a viral infection in a mammal, comprising: administering to said mammal a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a virus polynucleotide sequence necessary for replication and/or pathogenesis of said virus in an infected mammalian cell, in an amount effective to reduce or inhibit the function of said viral sequence upon subsequent introduction of said virus into said mammalian cells.

57. (original) A method for treatment or prophylaxis of a virally induced cancer in a mammal comprising: administering to said mammal a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a sequence encoding a tumor antigen, a regulatory sequence, or a functional fragment thereof, which antigen or sequence function is required for the maintenance of said tumor in said mammal, in an amount effective to reduce or inhibit the function of said antigen in said mammal.

58. (original) A method for the treatment or prophylaxis of infection of a mammal by an intracellular or extracellular pathogen comprising administering to said mammal a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a pathogenic or mammalian cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a polynucleotide sequence of said pathogen necessary for replication and/or

pathogenesis of said pathogen in an infected mammal or mammalian cell, in an amount effective to reduce or inhibit the ftinction of said sequence in said mammal.

59. (original) A method of treatment or prophylaxis of cancer in a mammal comprising administering to said mammal a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a polynucleotide sequence of an abnormal cancer-causing sequence in a mammal which also possesses a normal copy of said sequence, and wherein the differences between the abnormal sequence and said normal sequence are differences in polynucleotides, in an amount effective to reduce or inhibit the function of said abnormal sequence in said mammal.

60. (original) A method for treating a disease or disorder in a mammal comprising- administering to said mammal having a disease or disorder characterized by expression of polynucleotide product not found in a healthy mammal, a composition according to claim 1, wherein said target polynucleotide sequence is a polynucleotide sequence which expresses said polynucleotide product or regulatory sequence necessary to expression of said product, in an amount effective to reduce or inhibit the function of said target polynucleotide product in the cells of said mammal.

61. (original) Use of a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a

virus polynucleotide sequence necessary for replication and/or pathogenesis of said virus in an infected mammalian cell, in the preparation of a medicament for treating a viral infection in a mammal.

62. (original) Use according to claim 61, wherein said composition is in an amount effective to reduce or inhibit the function of said viral sequence in the cells of said mammal.

63. (original) Use according to claim 61, wherein said composition is in an amount effective to reduce or inhibit the function of said viral sequence upon subsequent introduction of said virus into said mammalian cells.

64. (original) Use of a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a sequence encoding a tumor antigen, a regulatory sequence, or a functional fragment thereof, which antigen or sequence function is required for the maintenance of said tumor in said mammal, in an amount effective to reduce or inhibit the function of said antigen in said mammal, in the preparation of a medicament for treatment or prophylaxis of a virally induced cancer in a mammal.

65. (original) Use of a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a pathogenic or mammalian cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a polynucleotide sequence of said pathogen

necessary for replication and/or pathogenesis of said pathogen in an infected mammal or mammalian cell, in an amount effective to reduce or inhibit the function of said sequence in said mammal, in the preparation of a medicament for the treatment or prophylaxis of infection of a mammal by an intracellular or extracellular pathogen.

66. (original) Use of a composition according to claim 1, with an optional second agent that facilitates polynucleotide uptake in a cell, in a pharmaceutically acceptable carrier, wherein said target polynucleotide is a polynucleotide sequence of an abnormal cancer-causing sequence in a mammal which also possesses a normal copy of said sequence, and wherein the differences between the abnormal sequence and said normal sequence are differences in polynucleotides, in an amount effective to reduce or inhibit the function of said abnormal sequence in said mammal, in the preparation of a medicament for the treatment or prophylaxis of cancer in a mammal.

67. (original) Use of a composition according to claim 1, wherein said target polynucleotide sequence is a polynucleotide sequence which expresses said polynucleotide product or regulatory sequence necessary to expression of a polynucleotide product not found in a healthy mammal, in an amount effective to reduce or inhibit the function of said target polynucleotide product in the cells of said mammal, in the preparation of a medicament for treating a disease or disorder in a mammal characterized by expression of said product.

68. (new) An isolated nucleic acid molecule comprising a regulatory sequence operably linked to a nucleic acid sequence that encodes an engineered ribonucleic acid (RNA) agent, wherein the agent comprises

(i) a first stem portion comprising a sequence of at least 18 nucleotides that is complementary to a sequence of a messenger RNA (mRNA) of a target gene;

(ii) a second stem portion comprising a sequence of at least 18 nucleotides that is sufficiently complementary to the first stem portion to hybridize with the first stem portion to form a duplex stem; and

(iii) a loop portion that connects the two stem portions.

69. (new) The nucleic acid molecule of claim 68, wherein the first stem portion is fully complementary to the mRNA sequence.

70. (new) The nucleic acid molecule of claim 68, wherein the second stem portion is fully so complementary to the first stem portion.

71. (new) The nucleic acid molecule of claim 68, wherein the first stem portion is located at a 5′ end of the RNA agent.

72. (new) The nucleic acid molecule of claim 68, wherein the first stem portion is located at a 3′ end of the RNA agent.

73. (new) The nucleic acid molecule of claim 68, wherein the loop portion comprises at least 4 nucleotides.

74. (new) The nucleic acid molecule of claim 68, wherein the loop portion comprises at least 7 nucleotides.

75. (new) The nucleic acid molecule of claim 68, wherein the loop portion comprises 11 nucleotides.

76. (new) The nucleic acid molecule of claim 68, wherein the sequence of the mRNA is located from 100 to 300 nucleotides 3' of the start of translation of the mRNA.

77. (new) The nucleic acid molecule of claim 68, wherein the sequence of the mRNA is located in a 5' untranslated region (UTR) or a 3' UTR of the mRNA.

78. (new) The nucleic acid molecule of claim 68, wherein the first and second stem portions each comprise about 18 to about 30 nucleotides.

79. (new) The nucleic acid molecule of claim 68, wherein the first and second stem portions each comprise about 22 to about 28 nucleotides.

80. (new) The nucleic acid molecule of claim 68, wherein the first and second stem portions each comprise the same number of nucleotides.

81. (new) The nucleic acid molecule of claim 68, wherein one of the first and second stem portions comprises 1 to 4 more nucleotides than the other stem portion.

82. (new) The nucleic acid molecule of claim 68, wherein the regulatory sequence comprises a Pol III or Pol II promoter.

83. (new) The nucleic acid molecule of claim 68, wherein the regulatory sequence is constitutive or inducible.

84. (new) A vector comprising the nucleic acid molecule of claim 68.

85. (new) The vector of claim 84, wherein the vector is a plasmid or a viral vector.

86. (new) The vector of claim 85, wherein the viral vector is a retroviral vector.

87. (new) A host cell containing the nucleic acid molecule of claim 68.

88. (new) The host cell of claim 87, wherein the cell is a mammalian cell.

89. (new) A transgene comprising the nucleic acid of claim 68.

90. (new) An engineered RNA agent comprising

i) a first stem portion comprising a sequence of at least 18 nucleotides that is complementary to a sequence of a messenger RNA (mRNA) of a target gene;

ii)a second stem portion comprising a sequence of at least 18 nucleotides that is sufficiently complementary to the first stem portion to hybridize with the first stem portion to form a duplex stem; and

iii) a loop portion that connects the two stem portions.

91. (new) The agent of claim 90, wherein the first stem portion is fully complementary to the mRNA sequence.

92. (new) The agent of claim 90, wherein the second stem portion is fully complementary to the first stem portion.

93. (new) The agent of claim 90, wherein the first stem portion is located at a 5' end of the RNA agent.

94. (new) The agent of claim 90, wherein the first stem portion is located at a 3' end of the RNA agent.

95. (new) The agent of claim 90, wherein the loop portion comprises at least 4 nucleotides.

96. (new) The agent of claim 90, wherein the loop portion comprises at least 7 nucleotides.

97. (new) The agent of claim 90, wherein the loop portion comprises 11 nucleotides.

98. (new) The agent of claim 90, wherein the sequence of the mRNA is located in a 5′ untranslated region (UTR) or a 3′ UTR of the mRNA.

99. (new) The agent of claim 90, wherein the first and second stem portions each comprise about 18 to about 30 nucleotides.

100. (new) The agent of claim 90, wherein the first and second stem portions each comprise about 22 to about 28 nucleotides.

101. (new) The agent of claim 90, wherein the first and second stem portions each comprise the same number of nucleotides.

102. (new) The agent of claim 90, wherein one of the first and second stem portions comprises 1 to 4 more nucleotides than the other stem portion.

103. The agent of claim 90, wherein the target gene is a human gene.

104. (new) The agent of claim 90, wherein the target gene is a mutant human gene.

105. (new) The agent of claim 90, wherein the target gene is a viral gene.

106. (new) A method of inducing ribonucleic acid interference (RNAi) of a target gene in a cell, the method comprising

i) obtaining a host cell of claim 87;

ii) culturing the cell; and

iii) enabling the cell to express the RNA agent to form a small interfering ribonucleic acid (siRNA) within the cell, thereby inducing RNAi of the target gene in the cell.